

**ABSTRACT**

Dominant negative alleles of human mismatch repair genes can be used to generate hypermutable cells and organisms. By introducing these genes into cells and transgenic animals, new cell lines and animal varieties with novel and useful properties can be prepared more efficiently than by relying on the natural rate of mutation. Methods of generating mutations in genes of interest and of making various cells mismatch repair defective through the use of chemicals to block mismatch repair *in vivo* are disclosed.